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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,123	MARTIN ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Election 12/7/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *9,10,28-31 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-27,32,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/13/06 & 6/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-8, 11-27, 32 and new claims 34 and 35, in the reply filed on 12/7/05 is acknowledged. The traversal is on the ground(s) that all of the claims in the application involve related subject matter, e.g., a Neisserial surface proteins and, therefore, a search would comprise overlapping subject matter and would not place an undue burden on the Examiner. This is not found persuasive because The inventions of Groups I-III are biologically, chemically and structurally different from one another. The polypeptide of group I and polynucleotide of group II are patentably distinct inventions for the following reasons. Polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotide of group II does not necessarily encode a polypeptide of group I. For example, the polynucleotides of Group II include variant sequences which differ by as much as 30% from the coding sequence. Furthermore, the information provided by the polynucleotide of group I can be used to make a materially different polypeptide than that of group II. Searching the inventions of groups I and II together would impose a serious search burden. In the instant case, the search of the polypeptides and the polynucleotides are not coextensive. The inventions of Groups I and II have a separate status in the art as

shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. In addition, the polynucleotide claims include polynucleotides having 70% identity to the coding sequence identified. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. The scope of polynucleotides as claimed extend beyond the polynucleotide that encodes the claimed polypeptides as explained above; furthermore, a search of the nucleic acid molecules of claim 1(b) would require an oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptide of group II. As such, it would be burdensome to search the inventions of groups I and II together. See the Restriction Requirement of 6/6/05 for further detail.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 10, 28-31, and 33 are withdrawn from consideration since they are draw to a non-elected invention.

Sequence Compliance

2. It is noted that the instant specification also contains several nucleotide/amino acid sequences throughout the specification which are encompassed by the definitions

for nucleotide/amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) and which must conform with the sequence rules for all applications that include nucleotide/amino acid sequences. The sequence identifiers obtained through conformance (paper submission and CRF/electronic) must be inserted into the body of the specification directly following the sequence. The tables on pages 46-48 contain sequences which must comply, as well as the sequences embedded in the text on page 48, lines 20-21. Additionally, Applicants are responsible for meeting compliance with any sequence the Examiner may have inadvertently missed. APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-8, 11-27, 32, 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 4 are duplicate claims. The language is identical. One of the claims must be deleted.

Claim 1, 2-8, 11-12 are vague and indefinite due to the phrase "a liposome associated with at least one polypeptide". How is the liposome 'associated' with the polypeptide? Is the polypeptide incorporated to the liposome or is it attached in some other manner? Clarification and/or correction is required.

Claims 3 and 4 are vague and indefinite due to the terms 'fragment' and 'analog thereof'. because it is unclear what structure is encompassed by these terms. A 'fragment', 'analog' or derivative can read a single amino acid. The term analog encompass structures which are completely different from that of SEQ ID NO:2. With respect to the 'analog', it is unclear what structure is retained from the parent compound, SEQ ID NO:2. The metes and bounds of the claimed structures cannot be understood. The 'fragment', 'derivative' or 'analog' from the 'epitope bearing portion' of SEQ ID NO:2 is even more unclear. Correction and clarification is required.

Claim 6 is vague and indefinite due to the phrase 'epitope-bearing portion' because it is unclear which portions of the amino acid sequence bear epitopes. The specification is silent on the location of the epitopes. Accordingly, the claim is vague and indefinite.

Claims 7, 8 and 35 are vague and indefinite due to the percent homology recited in combination with 'fragments thereof'. A fragment reads on as few as one amino acid. Additionally, the "fragments thereof" are derived from polypeptide sequences that vary by as much as 30% from the known sequences, e.g., 70% homology. The current claim

language allows from these sequences to be drawn from the portion of the sequence that is unknown. The metes and bounds of the claimed molecule cannot be understood. In claim 8, the claimed polypeptides are drawn to a percent identity of an amino acid, but do not require these variable sequences to have a function. The metes and bounds of the claimed molecule cannot be understood. The current claim language allows from these sequences to be drawn from the portion of the sequence that is unknown. Appropriate correction is required.

Claim 32 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 32 provides for the use of 'a pharmaceutical method', but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 32 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example Ex parte Dunki, 153 USPQ 678 (Bd.App. 1967) and Clinical Products, Ltd. v. Brenner, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Additionally, claim 32 lacks antecedent basis for 'a pharmaceutical method according to claim 1". Claim 1 does not recite a 'pharmaceutical method". Claim 1 is directed to a 'pharmaceutical composition'. Appropriate correction is required.

Claim Rejections - 35 USC § 112-Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The instant claims are drawn to pharmaceutical compositions comprising isolated polypeptides comprising amino acid sequences which are from 70-95% identical to SEQ ID Nos: 2. Fragments, analogues and derivatives from these variant sequences are also claimed. These terms can read on as few as one or more amino acids. Additionally, a fragment, analogue or derivative derived from an amino acid sequence which varies by as much as 30% identity from SEQ ID NOs:2, reads on fragments with nothing in common with SEQ ID NOs:2, e.g., the fragment, derivative or analogue could be taken from the 30% of the sequence which is different SEQ ID NOs:2. Methods of using these variant polypeptides or fragments, analogues and derivatives to protect/prevent against N.meningitidis, N.gonorrhoeae, N.lactamica and N.polysaccharea infection and/or to treat or protect against meningitidis and meningococcemia are also not enabled.

First, the breadth of the instant claims is drawn to polypeptides which are not specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what amino acids may be changed without

causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spatial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions.

The instant claims are drawn to proteins comprising a sequence with a given percent similarity to a protein. Selective point mutation to one key antigen could eliminate the ability of an antibody to recognize this altered antigen. If the range of decreased binding ability after single point mutation of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of protection/function, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of function. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool. Thus, proteins of different levels of homology may not induce antibody which is recognized by the native protein on the bacteria, and be ineffective in treating or preventing diseases or conditions caused by infection with

said bacteria. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different amino acid substitutions and the nature and extent of the changes that can be made. It is expensive and time consuming to make amino acid substitutions at more than one position, in a particular region of the protein, in view of the many fold possibilities for change in structure and the uncertainty as to what utility will be possessed. See Mikayama et al. (Nov.1993. Proc.Natl.Acad.Sci. USA, vol. 90 : 10056-10060) which teaches that the three-dimensional structure of molecules is important for their biological function and even a dingle amino acid difference may account for markedly different biological activities. Rudinger et al. (June 1976. Peptide Hormones. Biol.Council. pages 5-7) also teaches that amino acids owe their 'significance' to their inclusion in a pattern which is directly involved in recognition by, and binding to, the receptor and the significance of the particular amino acids and sequences for different amino acids cannot be predicted a priori, but must be determined from case to case by painstaking experimental study.

The specification is also not enabled for vaccines or methods of using the full-length proteins set forth in SEQ ID Nos: 2, variants of these polypeptides which differ are 70-95% identical to these sequences or fragments, analogues and derivatives derived from these polypeptides to protect against infection with N.meningitidis, N.gonorrhoeae, N.lactamica and N.polysaccharea, particularly meningitidis and meningococcemia. The bacterial vaccine and treatment art is highly unpredictable. The instant specification provides no results of treating or protecting these diseases,

particularly through the use of 'epitope-bearing portions, fragments, or variant polypeptides. In such an unpredictable art, specific evidences would need to be present in order to enable such a scope of invention.

The specification is not enabled for use of variant polypeptide sequences or fragments, derivatives or analogues in any of the claimed treatment methods or vaccines. The location of protective epitopes has not been identified. Often times it takes more than one epitope to provide a protective effect. As stated above, selective point mutation to one key antigen could eliminate the ability of an antibody to recognize this altered antigen. If the range of decreased binding ability after single point mutation of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of protection/function, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of function.

The instant specification provides no results of treating or protecting these diseases. In such an unpredictable art, specific evidences would need to be present in order to enable such a scope of invention. The specification does show some in vitro immunological assays using the full-length protein set forth in SEQ ID NO:2. However, these results do not enable in vivo methods and they do not enable use of fragments or analogs from SEQ ID NO:2.

Given the lack of guidance contained in the specification, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112-Written Description

6. Claims 3-8, 32, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:2 and antigenic portions from this sequence. Therefore, the written description is not commensurate in scope with the claims which encompass variants of SEQ ID NO:2 or fragments from sequences with 70-95% homology to SEQ ID NO:2.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO: 2 and its immunogenic fragments, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a

potential method of isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore, the full breadth of the claims does not meet the written description provisions of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-8, 11-27, 32, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brodeur et al (WO 96/29412) in view of anyone of Ward et al

(Microbial Pathogenesis. 1996. 21: 499-512), Idanpaan-Heikkila et al (Vaccine. 1995. 13(16): 1501-8), or Wright et al (Infection and Immunity, August 2002, 70(8): 4028-4034).

Brodeur et al teach an isolated outer membrane protein from *Neisseria meningitidis* which is 100% identical to the protein taught by Applicant's as SEQ ID NO: 2. Fragments of this protein are also taught as well as methods for producing it recombinantly. See top of page 6 and pages 18-19. It is taught that the protein may be used in prophylactic and diagnostic compositions and methods useful in the treatment, prevention and diagnosis of *Neisseria meningitidis*. See abstract. Hybrid or chimeric proteins are also taught. Brodeur et al teach that this protein is highly conserved.

However, Brodeur et al do not specifically teach the use of a liposome with their polypeptide.

Ward et al teach that the incorporation of isolated *N.meningitidis* proteins into liposomes allows for the proteins to achieve optimal protein folding. It is taught that the use of liposomes replaced the use of LPS to promote native-like folding of the protein to an active conformation without the negative toxic effects associated with LPS. The use of adjuvants such as monophosporyl lipid A or muramyl dipeptide along with the liposomes is specifically taught. However, it is taught that an effective bactericidal response was obtained with the purest preparation of protein incorporated into liposomes. Page 503 teaches how to incorporate the proteins into liposomes. Liposomes composed of phosphatidylcholine and cholesterol are taught. Page 508 teaches that the advantage of using liposomes is primarily the potential for folding of the

protein in the liposomal membrane to a native-like conformation and the inherent immunoadjuvant activity of the liposome vesicles.

Idanpaan-Heikkila et al teach that when the outer membrane protein P1 from *N.meningitidis* was reconstituted with of phosphatidylcholine into liposomes, native antigenic epitopes were formed. It is taught that the liposomes were reproducibly immunogenic at a low dose without any other adjuvant. The antibodies produced were both bactericidal and protective against infection in the infant rat model.

Wright et al teach the incorporation of the recombinant PorB outer membrane protein of N.meningitidis into liposomes for use as a vaccine. The liposome preparations proved to induce a much greater immune response than the PorB adsorbed to $Al(OH)_3$. It is further taught that reactivity with native protein was considerably enhanced by incorporation of the adjuvant monophosporyl lipid A into the liposome. See abstract.

It would have been prima facie obvious to incorporate the isolated *N.meningitidis* protein taught by Brodeur et al (which is the same as the protein taught by Applicant's as SEQ ID NO:2) or its immunogenic fragments thereof, as well as fusion or chimerics of said protein, into liposomes because the prior art, as evidenced by Ward, Idanpaan-Heikkila et al, and Wright, extensively taught that incorporating isolated, denatured or recombinant *N.meningitidis* proteins into liposomes allows for the proteins to achieve optimal protein folding which allowed for native-like conformation. It is taught that the use of liposomes replaced the use of LPS to promote native-like folding of the protein to an active conformation without the negative toxic effects associated with LPS. One of

ordinary skill in the art would have been motivated to incorporate the protein taught by Brodeur into liposomes because doing so not only allows for the protein to obtain native-like conformation, but also has the added benefit of the inherent immunoadjuvant activity of the liposome vesicles. The secondary references further teach that the liposomes may be used with or without a further adjuvant. The protein taught by Brodeur et al would inherently comprise an 'epitope-bearing portion'. The doses taught in instant claim 27 is consistent with what is taught by Brodeur et al.

8. Claims 1-8, 13-27, 32, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Cadieux et al (Infect. Immun. Sept. 1999. 67(9): 4955-4959), Plante et al (Infect. Immun. June 1999. 67(6): 2855-2861) or Martin et al (J.Exp.Med. 1997. 185(7): 1173-1183) in view of anyone of Ward et al (Microbial Pathogenesis. 1996. 21: 499-512), Idanpaan-Heikkila et al (Vaccine. 1995. 13(16): 1501-8), or Wright et al (Infection and Immunity, August 2002, 70(8): 4028-4034).

Cadieux et al, Martin et al and Plante et al teach an isolated surface protein from *Neisseria meningitidis* which is 100% identical to the protein taught by Applicant's as SEQ ID NO: 2. Fragments of this protein are also taught as well as methods for producing it recombinantly. The references teach that the protein is highly conserved and is capable of protecting against meningococcal infections.

However, Cadieux et al, Martin et al and Plante et al do not specifically teach the use of a liposome with their polypeptide.

Ward et al teach that the incorporation of isolated *N.meningitidis* proteins into liposomes allows for the proteins to achieve optimal protein folding. It is taught that the

use of liposomes replaced the use of LPS to promote native-like folding of the protein to an active conformation without the negative toxic effects associated with LPS. The use of adjuvants such as monophosporyl lipid A or muramyl dipeptide along with the liposomes is specifically taught. However, it is taught that an effective bactericidal response was obtained with the purest preparation of protein incorporated into liposomes. Page 503 teaches how to incorporate the proteins into liposomes. Liposomes composed of phosphatidylcholine and cholesterol are taught. Page 508 teaches that the advantage of using liposomes is primarily the potential for folding of the protein in the liposomal membrane to a native-like conformation and the inherent immunoadjuvant activity of the liposome vesicles.

Idanpaan-Heikkila et al teach that when the outer membrane protein P1 from *N.meningitidis* was reconstituted with of phosphatidylcholine into liposomes, native antigenic epitopes were formed. It is taught that the liposomes were reproducibly immunogenic at a low dose without any other adjuvant. The antibodies produced were both bactericidal and protective against infection in the infant rat model.

Wright et al teach the incorporation of the recombinant PorB outer membrane protein of N.meningitidis into liposomes for use as a vaccine. The liposome preparations proved to induce a much greater immune response than the PorB adsorbed to $Al(OH)_3$. It is further taught that reactivity with native protein was considerably enhanced by incorporation of the adjuvant monophosporyl lipid A into the liposome. See abstract.

It would have been prima facie obvious to incorporate the isolated *N.meningitidis* protein taught by any one of Cadieux et al, Martin et al or Plante et al (which is the same as the protein taught by Applicant's as SEQ ID NO:2), into liposomes because the prior art, as evidenced by Ward, Idanpaan-Heikkila et al, and Wright, extensively taught that incorporating isolated, denatured or recombinant *N.meningitidis* proteins into liposomes allows for the proteins to achieve optimal protein folding which allowed for native-like conformation. It is taught that the use of liposomes replaced the use of LPS to promote native-like folding of the protein to an active conformation without the negative toxic effects associated with LPS. One of ordinary skill in the art would have been motivated to incorporate the protein taught by Cadieux et al, Martin et al and Plante et al into liposomes because doing so not only allows for the protein to obtain native-like conformation, but also has the added benefit of the inherent immunoadjuvant activity of the liposome vesicles. The secondary references further teach that the liposomes may be used with or without a further adjuvant. The protein taught by Cadieux et al, Martin et al and Plante et al would inherently comprise an 'epitope-bearing portion'. The doses taught in instant claim 27 is consistent with what is taught by Brodeur et al.

9. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571)

272-0858. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

3/1/06